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09/880,688	06/13/2001	Annemarie Poustka	POUSTKA-2	6614

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/880,688	POUSTKA ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-60,66-71,75,78-82 and 84-87* is/are pending in the application.

4a) Of the above claim(s) *68 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-60,66,67,75,78-82,84,86 and 87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Prosecution of the application is reopened in view of the conference held with supervisor Christopher Low (please see the letter mailed on 2/24/10). The finality of the last Office action is withdrawn and a new Office action is issued below.

Status of Claims

Claim 56-60, 66-71, 75, 78-82 and 84-87 are pending in the instant application.

Claims 1-55, 61-65, 72-74, 76-77 and 83 have been cancelled.

Claims 68 and 85 are withdrawn from further consideration as being drawn to non-elected invention.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84 and 86-87 are under examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on 12/14/1998 and 7/30/1999. It is noted, however, that applicant has not filed a certified copy of the GERMANY 198 57 529.7 and GERMANY 199 35 553.3 applications as required by 35 U.S.C. 119(b). Therefore, the filing date of the instant application is deemed

to the filing date of the PCT/DE99/03982 application of **December 14, 1999.**

Claim Objections

Claims 56-60, 66-67 and 69-71 are objected to because of the following informalities:

Claims 56-60, 66-67, 69-71 improperly depend on the higher claim number 75. A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. See MPEP § 608.01(n).

[Please note that claim 83, which has been cancelled, is improperly included as the last line of claim 82].

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56-60, 66-67, 69-71, 75(amended), 78-82, 84, 86 and new claim 87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter Rejection

The following amendments in claim 75 do not find support in the as-filed specification:

1). “Embedding of monomers within a solvent”,

2). “Washing away transport units”,

3). “Changing the transports units from a solid state of aggregation to a liquid state of aggregation” and,

4). The entire claim 87.

MPEP 2163.06 clearly states that applicants point out where in the specification support for the newly added limitations can be found.

Written Description Rejection

Claims 56-60, 66-67, 69-71, 75(amended), 78-82, 84, 86 and new claim 87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Moba, B.V. v.Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.

The specification fails to describe the method steps of embedding at least two different amino acid monomers or oligonucleotide monomers at a temperature of less than 90° C within a solvent that is in a solid state of aggregation,

thereby forming monomer-immobilizing transport units. It is not apparent from the as-filed disclosure how the different monomers are embedded within a solvent that is in a solid state of aggregation. Furthermore, there is no detail description of any solvent(s) that is in a solid state of aggregation at said temperature. The specification merely provides the definition at e.g., page 1, paragraph [0009] that the term "solid state of aggregation" also includes undercooled liquids. The definition is confusing in that it failed not only to define the kind/type of solvent in the solid state of aggregation but also what is included or precluded in the undercooled liquids. The specification describes the solvent in terms of the single solvent diphenylformamide, e.g., page 4, paragraph [0051]. There is no description as to how the single solvent is embedded with the monomers at the given temperature. Furthermore, it does not describe how this single solvent represents the numerous solvents covered by the huge genus solvents. The general statements in the specification are therefore not a detail description of the invention.

A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it

from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84, 86 and new claim 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 75 recitation of the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

2. Claim 75 is being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: changing the transport

units from a solid to a liquid state of aggregation. It is not clear whether simply mobilizing and diffusing the monomers changed the transport units from a solid state of aggregation to a liquid state of aggregation.

3. Claim 75 is unclear with the amendment cancelling "matrix". It is unclear how a monomer is embedded in a liquid that is in a solid state of aggregation, especially in the absence of positive support in the as-filed specification.

4. The term "defined" in claims 75, 80 and 87 are relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear how the monomers are considered to be "defined" in a position given that the transport units are applied to the entire support. It is not clear as to the characterizing/distinguishing features of a defined location.

5. The inconsistent used of different terminologies, 'solvent in a solid state of aggregation" in claim 75, "transport units" in claim 80 and "matrix", to mean the same

thing, if indeed this is so, provides for confusion and ambiguity. While applicant is permitted to be his own lexicographer however, it carries with it the connotation that he will use terms consistently throughout his patent. Porter v. Farmers Supply Services Inc., 228 USPQ 4.

6. In claim 80, “repeatedly applying” is vague and indefinite as to the repetitive application of the monomers in the same (defined location). The entire step itself, as amended, is indefinite.

7. The term "deep-frozen” in claim 66 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the depth of freezing are not clearly set forth in the specification.

8. Claim 67 recites “derivatives”, the metes and bounds of which are vague and indefinite. It is indefinite as to the type/kind of derivatives or molecules being derivatized and/or the kind of derivatizing molecules.

This rejection has the same import to claim 87.

9. Claim 67 is an improper Markush grouping of compounds. The compounds do not seem have a common property among the members of the groups. See MPEP 803.02.

10. Claim 69 is vague and indefinite as to the preliminary stage of a monomer. It is not clear as to what would be considered a preliminary stage of a monomer.

11. Claim 71 is unclear as to the fragments being applied to the support by e.g., **magnetic means**. This is being inconsistent with the base claim applying by laser printing.

12. Claim 87 is unclear as to the metes and bounds of "a matrix" especially as to the embedding, absent positive support in the specification. The metes and bounds of said matrix is not clearly set forth in the claim as set forth in the last Office action.

Response to Arguments

Applicant states that claim 75 has been amended to refer to the definition of FIG. 25 in which the matrix is schematically seen. The numeral listing also includes the term matrix.

"Matrix" is for example defined among others as "a mass by which something is enclosed or embedded". See Webster Third New International Dictionary. Here the matrix included the solvent as now recited in the claim. The support is where the monomers are being coupled to after the mobilization step.

In reply, there is no Fig. 25 in the instant specification. The definition of a matrix is not controverted, albeit the metes and bounds of said “mass” as applied to the instant claim is also vague. The issue is the matrix as claimed is indefinite as to what is included or precluded by said matrix (or mass to which something is enclosed or embedded).

13. The steps in claim 87 do not seem to correspond with one another as there seems to be a missing element(s) or step(s).

14. The term "suitable" in claim 87 is a relative term which renders the claim indefinite. The term "suitable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is vague and indefinite as to what are the features of an amino acid to be considered “suitable" for synthesis.

Claim Rejections - 35 USC § 102/35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The text of those sections of Title 35, U.S. Code 103 not included in this action can be found in a prior Office action.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84 and 86-87 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Blanchard (USP 6028189)(as evident by The Condensed Chemical Dictionary).

For claims 56-58, 66, 67, 69, 71, 75, 80-82, 84 and 86; Blanchard discloses throughout the patent at e.g., col. 2, line 46 up to col. 4, line 30, a method of oligonucleotide synthesis comprising chemically coupling a first nucleotide monomer to a second nucleotide monomer in a high surface tension solvent (i.e., embedding step with a solvent in state of aggregation, as claimed in e.g., claim 75). Blanchard discloses the step-by-step synthesis at e.g., col. 3, lines 19-50 which comprises: (a) applying at least a first reagent dissolved in propylene carbonate to said surface, wherein said substrate is chemically prepared to react with said first reagent to covalently attached said reagent to said substrate; (b) applying at least one either the first reagent or a second reagent dissolved in propylene carbonate to said surface wherein said substrate is chemically prepared to react with said reagent to covalently attach said reagent to said substrate; (c) optionally repeating step (b) at least one time using the same or different reagents dissolved in propylene carbonate wherein each of said reagents covalently attaches to said substrate to form covalently attached compounds; (d) washing said substrate to remove unattached reagents; (e) modifying said attached reagents; and (f) repeating steps (a) through (e) at least once with the same or

different reagents dissolved in propylene carbonate at various loci on the substrate. Using the above method, a plurality(library as claimed) of different chemical compounds within the array can be simultaneously synthesized.

Blanchard discloses at e.g., col. 3, lines 2-5, an automated assembly of the oligonucleotides into the array using an ink-jet pump apparatus to deliver the first and second nucleotide monomers to a specified position on a solid support.Blanchard further discloses at e.g., col. 8, lines 15-18, application of reagent to the wells using e.g., an ink-jet printer, a laser printer with a soluble toner, evaporation or by a photolithographic process.

For claims 56-60 and 66, Balnchard discloses the propylene carbonate, (reads on the claim solvent in solid state of aggregation) which is supercooled (undercooled) liquid at a temperature of -49oC (please see the Condensed Chemical Dictionary).

For claim 69, Blanchard discloses at e.g., col. 6, lines 5-8, “to extend the chain, one of the two terminal protecting groups must be removed selectively to generate a free hydroxyl function to which a new partially protected unit can be joined.”

(Noteworthy is applicants' claim 69 that claims "detaching protective groups by **standard methods**"). (Emphasis ours.)

For claim 70, Blanchard discloses at e.g., col. 5, line 12-18, the substrate as paper or polystyrene.

For claim 71, Blanchard discloses at e.g., Figure 2 a transient voltage applied to the piezoelectric actuator.

The claim temperature of the solvent in solid state of aggregation is a property considered inherent to the compound of Blanchard i.e., propylene carbonate which is an undercooled liquid at -42oC.

Claim Rejections - 35 USC § 103

Claims 56-60, 66-67, 75, 78-82, 84, 86 as amended and new claim 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (USP 6028189) in view of Zebala (USP 6951682) and Anderson et al (USP 7179638).

For claims 56-58, 66, 67, 69, 71, 75, 80-82, 84 and 86; Blanchard discloses throughout the patent at e.g., col. 2, line 46 up to col. 4, line 30, a method of oligonucleotide synthesis comprising chemically coupling a first nucleotide monomer to a second nucleotide monomer in a high surface tension solvent (i.e., embedding step with a solvent in state of aggregation, as

claimed in e.g., claim 75). Blanchard discloses the step-by-step synthesis at e.g., col. 3, lines 19-50 which comprises: (a) applying at least a first reagent dissolved in propylene carbonate to said surface, wherein said substrate is chemically prepared to react with said first reagent to covalently attached said reagent to said substrate; (b) applying at least one either the first reagent or a second reagent dissolved in propylene carbonate to said surface wherein said substrate is chemically prepared to react with said reagent to covalently attach said reagent to said substrate; (c) optionally repeating step (b) at least one time using the same or different reagents dissolved in propylene carbonate wherein each of said reagents covalently attaches to said substrate to form covalently attached compounds; (d) washing said substrate to remove unattached reagents; (e) modifying said attached reagents; and (f) repeating steps (a) through (e) at least once with the same or different reagents dissolved in propylene carbonate at various loci on the substrate. Using the above method, a plurality (library as claimed) of different chemical compounds within the array can be simultaneously synthesized.

Blanchard discloses at e.g., col. 3, lines 2-5, an automated assembly of the oligonucleotides into the array using an ink-jet pump apparatus to deliver the first and second

nucleotide monomers to a specified position on a solid support. Blanchard further discloses at e.g., col. 8, lines 15-18, application of reagent to the wells using e.g., an ink-jet printer, a laser printer with a soluble toner, evaporation or by a photolithographic process.

For claims 56-60 and 66, Blanchard discloses the propylene carbonate, (reads on the claim solvent in solid state of aggregation) which is supercooled (undercooled) liquid at a temperature of -49oC (please see the Condensed Chemical Dictionary).

For claim 69, Blanchard discloses at e.g., col. 6, lines 5-8, "to extend the chain, one of the two terminal protecting groups must be removed selectively to generate a free hydroxyl function to which a new partially protected unit can be joined." {Noteworthy is applicants' claim 69 that claims "detaching protective groups by **standard methods**"). (Emphasis ours.)

For claim 70, Blanchard discloses at e.g., col. 5, line 12-18, the substrate as paper or polystyrene.

For claim 71, Blanchard discloses at e.g., Figure 2 a transient voltage applied to the piezoelectric actuator.

Blanchard does not expressly disclose a matrix by which the nucleic acid is embedded including the solvent at a temperature of less than 90oC as in claim 87 or the temperature in a range of -10oC and 80oC as in claim 78 or 0oc and 40oC as in claim 79. However, Zebala discloses at e.g., col. 72, lines 1-20; polymeric films contain one or more receptors and/or indicator compounds in a polymer matrix comprising, for example, polyvinyl alcohol or any other such polymer compatible with detecting binding of particular ligands and receptors. In some embodiments, the films will be photopatternable, and will typically swell when hydrated forming a polymeric gel. After either chemical or photolytic release from the support, ligands will diffuse into the surrounding gel matrix. If a particular group of ligands specifically binds the receptors in the gel, then a zone of activity will be visible around that group. Determining the position of the element will reveal the reagent history, or more preferably, the composition of the ligand in a straightforward fashion.

Anderson discloses at e.g., col. 13, lines 35-50 that solidifying matrix holding the reagent(s) may be dissolvable, meltable, degradable, or reversible to further enhance interaction. Anderson further discloses at e.g., col. 36, lines

63 up to col. 37, line 6 porous particles (with many internal crevices), has a diameter of approximately 5 microns. Attached proteins are distributed over the internal surfaces as well as the exterior surface of the particle. By embedding the particles in a suitable medium, a sliceable solid matrix in which the antibody was immobilized and fairly uniformly distributed was created. By exploiting the 3-dimensional nature of the support, a slice containing such particles offers greater capacity (for antibody and thus for antigen binding).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to embed the solvent aggregating monomer in a matrix in the method of Blanchard as taught by Zebala and Anderson. One would have a reasonable expectation of success since different components/substances have been deposited into an array by a matrix which contains the compound or reagent of interest. A compound/substance in a matrix, makes the compound e.g., antibody fairly uniformly distributed on the array. A support containing a particle in a matrix offers greater capacity for compound interaction as taught by Anderson. Zebala teaches the conventionality of using a matrix containing a substance in a solvent. Blanchard likewise suggests that matrix in an array has

been used in the art citing e.g., Brennan. One having ordinary skill in the art would have a reasonable expectation of success in using a matrix to deposit in an array a compound therein as successfully shown by the different cited prior art above. A compound embedded in a matrix provides for a uniform distribution of said compound when applied to a surface.

The claim temperature of the solvent is a result effective variable well within one of ordinary skill in the art to determine. Said temperature, if not an inherent property of the solvent at hand, would be within one of ordinary skill in the art to determine.

The claim method of synthesizing monomers by depositing a solvent containing the compound being synthesized on an array using either an ink-jet or laser printer is well-practiced in the art at the time of the invention.

> If a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639